Sage Therapeutics Announces Third Quarter 2022 Financial Results and Highlights Pipeline and Business Progress

November 8, 2022

Completion of rolling NDA submission for zuranolone in MDD and PPD on track for December 2022

Presented additional data across pipeline programs at key medical congresses including data on zuranolone as an investigational oral, once-daily, 14-day treatment for MDD and PPD

Company appoints Laura Gault, M.D., Ph.D., as Chief Medical Officer, enhancing management team and advancing Sage's position as a leader in brain health and a top-tier biopharmaceutical company

Cash and cash equivalents, anticipated funding from ongoing collaborations, and potential revenue, expected to support operations into 2025

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Nov. 8, 2022-- Sage Therapeutics, Inc. (Nasdaq: SAGE), a biopharmaceutical company leading the way to create a world with better brain health, today reported business highlights and financial results for the third quarter ended September 30, 2022.

"This has been an important year for Sage, marked by the execution of significant milestones across our franchises. Looking ahead, we remain focused on the completion of the NDA submission for zuranolone in MDD and PPD, and are well into commercialization preparations to support a potential launch. Patients with depression are desperate to find new medicines that are safe, rapid-acting, short course, and have a sustained effect. We believe zuranolone, if approved, has the potential to deliver a new treatment option for patients," said Barry Greene, Chief Executive Officer at Sage Therapeutics. "In parallel, our team is advancing multiple clinical studies across our pipeline that span our neuropsychiatry and neurology franchises. I am proud of the tremendous progress our team has made on behalf of patients this year and am energized by the momentum we have going into 2023 and beyond."

Third Quarter 2022 Portfolio Updates

Sage is advancing a portfolio of clinical programs featuring internally discovered novel chemical entities with the potential to become differentiated products designed to improve brain health by targeting the $GABA_A$ and NMDA receptor systems. Dysfunction in these systems is thought to be at the core of numerous neurological and neuropsychiatric disorders.

Depression Franchise

Sage's depression franchise features zuranolone, Sage's next-generation positive allosteric modulator (PAM) of $GABA_A$ receptors being evaluated in clinical development as a treatment for various affective disorders, and ZULRESSO® (brexanolone) CIV injection, approved by the U.S. Food and Drug Association (FDA) as the first treatment specifically indicated for postpartum depression (PPD). Zuranolone has received Breakthrough Therapy and Fast Track Designation for the treatment of major depressive disorder (MDD) and Fast Track Designation for the treatment of PPD from the FDA.

Zuranolone is being evaluated as a potential rapid-acting, once-daily, oral two-week treatment for MDD and PPD in the LANDSCAPE and NEST clinical development programs, respectively. Across seven positive clinical trials, zuranolone has demonstrated rapid and sustained relief of depressive symptoms in people with MDD and PPD.

In the third quarter, Sage and its collaborator, Biogen, announced multiple new analyses across the development program for zuranolone, presented at the 2022 Psych Congress and the 35th European College of Neuropsychopharmacology (ECNP) Congress. The presentations included new analyses from the SHORELINE Study and Health Economics and Outcomes Research, as well as the first presentation of data from the SKYLARK Study.

Sage and Biogen continue to advance a rolling NDA submission for zuranolone for the treatment of both MDD and PPD, which is on track to be completed in December 2022.

The Company expects to achieve the following milestones across its depression franchise in 2022:

- Late 2022:
  - Complete NDA submission for zuranolone in MDD and PPD (December 2022).
  - Additional presentations of zuranolone data throughout 2022.

Neuropsychiatry Franchise

Sage's neuropsychiatry franchise features SAGE-718, the Company's first-in-class NMDA receptor PAM and lead neuropsychiatric drug candidate, in development as a potential oral therapy for cognitive disorders associated with NMDA receptor dysfunction, potentially including Huntington's disease (HD), Parkinson's disease (PD) and Alzheimer's disease (AD). SAGE-718 received Fast Track Designation from the FDA for development as a potential treatment for HD.

Sage is advancing a robust clinical program for SAGE-718 with multiple ongoing or planned Phase 2 studies, including the DIMENSION and

SURVEYOR Studies in people with HD cognitive impairment, the lead indication for SAGE-718, the PRECEDENT Study in people with mild cognitive impairment (MCI) associated with PD and the LIGHTWAVE Study in people with MCI and mild dementia due to AD. Sage is currently enrolling in the following Phase 2 studies:

- DIMENSION (CIH-201) Study: The DIMENSION Study is a double-blind, placebo-controlled study in people with HD cognitive impairment. The study is designed to evaluate the efficacy of once-daily SAGE-718 dosed over three months, with a target enrollment of approximately 178 people. Sage expects the DIMENSION Study to include more than 40 clinical sites.
- SURVEYOR (CIH-202) Study: The SURVEYOR Study is a double-blind, placebo-controlled study in people with HD cognitive impairment and healthy volunteers, with the goal of generating evidence linking efficacy signals on cognitive performance to domains of real-world functioning.
- PRECEDENT (CNP-202) Study: The PRECEDENT Study is a double-blind, placebo-controlled study in people with MCI due to PD. The study is designed to evaluate the safety and efficacy of SAGE-718 in people with MCI due to PD over 42 days, followed by a controlled follow-up period.

The Company expects to achieve the following milestones across its neuropsychiatry franchise in 2022:

- Late 2022:
  - Phase 3 Open-label Safety Study in HD (CIH-301): Initiate an open-label Phase 3 safety study of SAGE-718 in people with HD cognitive impairment.
  - LIGHTWAVE (CNA-202) Study: Initiate a placebo-controlled Phase 2 study of SAGE-718 in people with mild cognitive impairment and mild dementia due to AD.
  - Present additional SAGE-718 data throughout 2022.

Neurology Franchise

Sage's neurology franchise features SAGE-324 and SAGE-689. SAGE-324, a next-generation PAM of $GABA_A$ receptors and Sage's lead neurology program, is in development as a potential oral therapy for neurological conditions, such as essential tremor (ET), epilepsy and PD. SAGE-689 is an intramuscular $GABA_A$ receptor PAM in development as a potential therapy for disorders associated with acute GABA hypofunction.

Sage and its collaborator, Biogen, are currently enrolling participants in the Phase 2b KINETIC 2 placebo-controlled study of SAGE-324 in ET following positive results from the KINETIC Study. The KINETIC 2 Study is a Phase 2b dose-ranging study with the primary goal of defining the dose for SAGE-324 in ET with a good tolerability profile and a dosing schedule to maintain plasma concentrations needed for sustained tremor symptom control in treating ET. Enrollment in the KINETIC 2 Study is now expected to be completed in late 2023 due to a slower than anticipated pace of enrollment.

Sage is also currently dosing patients in a Phase 2 long-term open label safety study, to evaluate the long-term safety and tolerability of SAGE-324 in ET. The primary endpoint is incidence of treatment-emergent adverse events.

SAGE-689 continues in Phase 1 development.

Early Development

Sage is progressing its early development programs with IND-enabling work underway for SAGE-319 and SAGE-421.

- **SAGE-319:** an oral, extrasynaptic $GABA_A$ receptor preferring PAM that Sage plans to study for potential use in disorders of social interaction.
- **SAGE-421:** an oral, NMDA receptor PAM that Sage plans to study for potential use in neurodevelopmental disorders and cognitive recovery and rehabilitation.

Business Updates

During the third quarter, Sage announced key leadership changes:

- **Laura Gault,** M.D., Ph.D., joined Sage as Chief Medical Officer. As a part of her new role, Laura will be focused on advancing Sage's current and emerging product pipeline through all stages of development. Laura brings more than 15 years of experience with an established track record of neuroscience drug development and designing innovative clinical trial designs.
- **Jeff Jonas**, transitioning from his full-time role as Chief Innovation Officer at Sage and will continue as a member of the Board of Directors and other committees. Jeff will be pursuing a new opportunity at a global private equity firm.

FINANCIAL RESULTS FOR THE THIRD QUARTER 2022

- **Cash Position**: Cash, cash equivalents and marketable securities as of September 30, 2022 were $1.4 billion compared to $1.5 billion at June 30, 2022.
- **Revenue**: Net revenue from sales of ZULRESSO was $1.7 million in the third quarter of 2022, compared to $1.4 million in

the same period of 2021.

- **R&D Expenses:** Research and development expenses were $81.6 million, including $6.0 million of non-cash stock-based compensation expense, in the third quarter of 2022 compared to $83.5 million, including $17.9 million of non-cash stock-based compensation expense, for the same period in 2021. The decrease in R&D expenses was primarily due to the completion of the WATERFALL Study and the CORAL Study for zuranolone and decreases in non-cash stock-based compensation expense. Decreases were primarily offset by increased spending on SAGE-324 and Sage's wholly owned pipeline, including SAGE-718 and other programs. The reimbursement from Biogen for R&D expenses pursuant to the Sage/Biogen Collaboration and License Agreement was $17.9 million in the third quarter of 2022 compared to $21.6 million in the same period of 2021.

- **SG&A Expenses**: Selling, general and administrative expenses were $61.5 million, including $7.2 million of non-cash stock-based compensation expense, in the third quarter of 2022, compared to $48.7 million, including $16.5 million of non-cash stock-based compensation expense, for the same period in 2021. The increase in SG&A expenses was primarily due to hiring employees to support ongoing activities in anticipation of potential future product launches of our product candidates. The reimbursement from Biogen for SG&A expenses pursuant to the Sage/Biogen Collaboration and License Agreement was $0.5 million in the third quarter of 2022 compared to $2.6 million in the same period of 2021.

- **Net Loss:** Net loss was $137.3 million for the third quarter of 2022 compared to $130.2 million for the same period of 2021.

FINANCIAL GUIDANCE

- Sage anticipates cash, cash equivalents and marketable securities of approximately $1.3 billion at the end of 2022.
- The Company does not anticipate receipt of any milestone payments from collaborations in 2022.
- The Company anticipates R&D and SG&A spending to increase as it advances planned and ongoing studies for SAGE-718 and SAGE-324 and prepares for the potential launch of zuranolone.
- The Company believes its cash and cash equivalents, anticipated funding from ongoing collaborations, and potential revenue, will support its operations into 2025.

Conference Call Information

Sage will host a conference call and webcast today, Tuesday, November 8, at 8:00 a.m. ET to review its third quarter 2022 financial results and discuss recent corporate updates. The live webcast can be accessed on the investor page of Sage's website at investor.sagerx.com. A replay of the webcast will be available on Sage's website following the completion of the event and will be archived for up to 30 days.

About Sage Therapeutics

Sage Therapeutics is a biopharmaceutical company fearlessly leading the way to create a world with better brain health. Our mission is to pioneer solutions to deliver life-changing brain health medicines, so every person can thrive. For more information, please visit www.sagerx.com.

Forward-Looking Statements

Various statements in this release concern Sage's future expectations, plans and prospects, including without limitation our statements regarding: plans and potential timing for completion of our rolling NDA submission for zuranolone in MDD and PPD; our belief in the regulatory filing and review pathway for zuranolone in MDD and PPD; the potential profile and benefit of zuranolone in MDD and PPD; the potential for regulatory approval and commencement of launch and commercialization of zuranolone; other planned next steps for the zuranolone program; anticipated timelines for commencement of trials, completion of dosing, initiation of new activities and other plans for our other programs and early stage pipeline; our belief in the potential profile and benefit of our product candidates; potential indications for our product candidates; the potential for success of our programs, and the opportunity to help patients in various indications; the mission and goals for our business; and our expectations with respect to 2022 year-end cash, no receipt of milestones from collaborations in 2022, funding of future operations and expectations for increases in expenses. These statements constitute forward-looking statements as that term is defined in the Private Securities Litigation Reform Act of 1995. These forward-looking statements are neither promises nor guarantees of future performance, and are subject to a variety of risks and uncertainties, many of which are beyond our control, which could cause actual results to differ materially from those contemplated in these forward-looking statements, including the risks that: we may experience delays or unexpected hurdles in our efforts to complete our rolling NDA submission for zuranolone in MDD and PPD and we may not be able to complete the submission on the timeline we expect or at all; the FDA may find inadequacies and deficiencies in our NDA for zuranolone, including in the data we submit, despite prior discussions, and may decide not to accept the NDA for filing; even if the FDA accepts the NDA for filing, the FDA may find that the data included in the NDA are not sufficient for approval and may not approve the NDA in MDD or PPD, or both; the FDA may decide that the design, conduct or results of our completed and ongoing clinical trials for zuranolone, even if positive, are not sufficient for approval in MDD or PPD and may require additional trials or data which may significantly delay and put at risk our efforts to obtain approval and may not be successful; even if our NDA is successfully filed and accepted, the FDA may not grant priority review or meet expected review timelines for our NDA; other decisions or actions of the FDA or other regulatory agencies may affect our efforts with respect to zuranolone and our plans, progress, results and expected timelines; results of ongoing or future studies may impact our ability to obtain approval of zuranolone or impair the potential profile of zuranolone; success in earlier clinical trials of any of our other product candidates may not be repeated or observed in ongoing or future studies, and ongoing and future clinical trials may not meet their primary or key secondary endpoints which may substantially impair development; unexpected concerns may arise from additional data, analysis or results from any of our completed studies; we may encounter adverse events at any stage that negatively impact further development, the potential for approval or the potential for successful commercialization of any our product candidates or that require additional nonclinical and clinical work which may not yield positive results; we may encounter delays in initiation, conduct, completion of enrollment or completion of our ongoing and planned clinical trials, including as a result of slower than expected site initiation, slower than expected

*enrollment, the need or decision to expand the trials or other changes, that may impact our ability to meet our expected timelines and increase our costs; decisions or actions of the FDA or other regulatory agencies may affect the initiation, timing, design, size, progress and cost of clinical trials and our ability to proceed with further development or may impair the potential for successful development; the anticipated benefits of our ongoing collaborations, including the achievement of events tied to milestone payments or the successful development or commercialization of products and generation of revenue, may never be achieved; the need to align with our collaborators may hamper or delay our development and commercialization efforts or increase our costs; our business may be adversely affected and our costs may increase if any of our key collaborators fails to perform its obligations or terminates our collaboration; the internal and external costs required for our ongoing and planned activities, and the resulting impact on expense and use of cash, may be higher than expected which may cause us to use cash more quickly than we expect or change or curtail some of our plans or both; we may never be able to generate meaningful revenues from sales of ZULRESSO or to generate revenues at levels we expect or at levels necessary to justify our investment; we may not be successful in our efforts to gain regulatory approval of products beyond ZULRESSO and, even if successfully developed and approved, we may not achieve revenues from such products, including zuranolone, if approved, at the levels we expect; our expectations as to year-end cash and sufficiency of cash to fund future operations and expense levels may prove not to be correct for these and other reasons such as changes in plans or actual events being different than our assumptions; we may be opportunistic in our future financing plans even if available cash is sufficient; additional funding may not be available on acceptable terms when we need it; the number of patients with the diseases or disorders for which our products are developed, the unmet need for additional treatment options and the potential market for our current or future products, including zuranolone, if approved, may be significantly smaller than we expect; ZULRESSO and zuranolone or any of our other products that may be approved in the future may not achieve market acceptance or we may encounter reimbursement-related or other market-related issues that impact the success of our commercialization efforts; and we may encounter technical and other unexpected hurdles in the development and manufacture of our product candidates or the commercialization of our marketed product which may delay our timing or change our plans, increase our costs or otherwise negatively impact our business; as well as those risks more fully discussed in the section entitled "Risk Factors" in our most recent quarterly report, as well as discussions of potential risks, uncertainties, and other important factors in our subsequent filings with the Securities and Exchange Commission. In addition, any forward-looking statements represent our views only as of today, and should not be relied upon as representing our views as of any subsequent date. We explicitly disclaim any obligation to update any forward-looking statements***.***

Financial Tables

Sage Therapeutics, Inc. and Subsidiaries
Condensed Consolidated Statements of Operations
(in thousands, except share and per share data)
(unaudited)

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2022	2021	2022	2021
Product revenue, net	$ 1,739	$ 1,440	$ 4,821	$ 4,666
Operating costs and expenses:				
Cost of goods sold	184	131	670	466
Research and development	81,553	83,497	236,868	207,723
Selling, general and administrative	61,482	48,706	160,370	131,899
Total operating costs and expenses	143,219	132,334	397,908	340,088
Loss from operations	(141,480)	(130,894)	(393,087)	(335,422)
Interest income, net	4,127	692	7,397	2,132
Other income, net	30	31	52	110
Net loss	$ (137,323)	$ (130,171)	$ (385,638)	$ (333,180)
Net loss per share - basic and diluted	$ (2.31)	$ (2.21)	$ (6.51)	$ (5.69)
Weighted average shares outstanding - basic and diluted	59,428,123	58,819,548	59,242,563	58,593,743

Sage Therapeutics, Inc. and Subsidiaries
Condensed Consolidated Balance Sheets
(in thousands)
(unaudited)

	September 30, 2022	December 31, 2021
Cash, cash equivalents and marketable securities	$ 1,393,639	$ 1,742,296
Total assets	$ 1,486,073	$ 1,825,288
Total liabilities	$ 105,951	$ 96,257
Total stockholders' equity	$ 1,380,122	$ 1,729,031

ZULRESSO (brexanolone) SELECT IMPORTANT SAFETY INFORMATION

This does not include all the information needed to use ZULRESSO safely and effectively. See full prescribing information for ZULRESSO.

WARNING: EXCESSIVE SEDATION AND SUDDEN LOSS OF CONSCIOUSNESS

See full prescribing information for complete boxed warning

Patients are at risk of excessive sedation or sudden loss of consciousness during administration of ZULRESSO.

Because of the risk of serious harm, patients must be monitored for excessive sedation and sudden loss of consciousness and have continuous pulse oximetry monitoring. Patients must be accompanied during interactions with their child(ren).

ZULRESSO is available only through a restricted program called the ZULRESSO REMS.

WARNINGS AND PRECAUTIONS

Suicidal Thoughts and Behaviors: Consider changing the therapeutic regimen, including discontinuing ZULRESSO, in patients whose PPD becomes worse or who experience emergent suicidal thoughts and behavior.

ADVERSE REACTIONS: Most common adverse reactions (incidence ≥5% and at least twice the rate of placebo) were sedation/somnolence, dry mouth, loss of consciousness, and flushing/hot flush.

USE IN SPECIFIC POPULATIONS

- **Pregnancy:** ZULRESSO may cause fetal harm. Healthcare providers are encouraged to register patients by calling the National Pregnancy Registry for Antidepressants at 1-844-405-6185 or visiting online at https://womensmentalhealth.org/clinical-and-researchprograms/pregnancyregistry/antidepressants/

- **Renal Impairment:** Avoid use of ZULRESSO in patients with end stage renal disease (ESRD)

Controlled Substance: ZULRESSO contains brexanolone, a Schedule IV controlled substance under the Controlled Substances Act.

To report SUSPECTED ADVERSE REACTIONS, contact Sage Therapeutics, Inc. at 1-844-4-SAGERX (1-844-472-4379) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see accompanying full Prescribing Information including Boxed Warning.

View source version on businesswire.com: https://www.businesswire.com/news/home/20221108005333/en/

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